

Relation Between Tumor Size and Range of Motion in IMRT Treatment Planning for Thoracic Lesions

Ivaylo B. Mihaylov^{1,2*}, Fritz A. Lerma³ and Eduardo G. Moros²

¹Department of Radiation Oncology, Rhode Island Hospital/ Warren Alpert Medical School of Brown University, 593 Eddy St., Providence, RI 02903

²Department of Radiation Oncology, University of Arkansas for Medical Sciences, 4301 W. Markham St., Little Rock, AR 72205

³Department of Radiation Oncology, University of Maryland School of Medicine, 22 South Greene Street, Baltimore, MD 21201

Abstract

Purpose: To evaluate the relation between tumor size/volume, tumor range of motion, and healthy lung volume in light of radiotherapy motion management paradigm.

Materials and Methods: Four patient data sets were considered in this investigation. Each patient underwent time resolved (4D) CT data scan. Mid-ventilation CT data sets, with nominal lung volumes ranging from ~3000 cm³ to ~6000 cm³, were considered for treatment planning. Spheres with pre-specified radii were auto-contoured in the left lower lobes as simulated planning target volumes (PTVs) for each patient. Motion in superior-inferior direction was superimposed on the simulated spherical PTVs, such that motion-inclusive ITV_s were generated. Nine-field IMRT treatment plans were created for all lung volumes, different combinations of simulated PTV spherical size and ranges of motion. Three dose levels of 60 Gy, 70 Gy, and 80 Gy were utilized. The doses were prescribed to 95% of the ITV. Simulated PTV sizes and ranges of motion were varied until prescriptions were met, given that organs at risk (OARs) were spared. The OAR constraints were: 40 Gy to 1% of the cord and 30% of the heart, as well as 20 Gy and 30 Gy to 30% and 20% of benign lung, respectively. These constraints, representative for 2 Gy per fraction fractionation schemes, are commonly used clinically. The treatment plans were deemed clinically acceptable when standard deviation of the dose across the ITV was less than 3% of the prescription dose in addition to fulfillment of the OAR constraints.

Results: For each nominal lung volume three look-up curves, corresponding to the prescription dose levels were generated. The plots related the PTV sphere sizes with its range of motion. In addition, correlation between the absolute tumor volume and its range of motion was also established and presented in graphical format.

Conclusions: The motion management threshold of 0.5 cm found in the literature is reasonable. However, in some cases, depending on the tumor size, tumor range of motion, and nominal lung volumes, it might be too restrictive. In the determination of the most appropriate individualized treatment planning approach all factors such as tumor and lung volumes, tumor range of motion and patient tolerance toward the treatment technique need to be assessed.

Keywords: Motion management; 4D; Dose; IMRT; Lung

Introduction

Respiration causes tumors in the thoracic and the abdominal cavities to move appreciably in all directions. (Britton et al., 2007; Ionascu et al., 2007; Seppenwoolde et al., 2002; Shimizu et al., 2001; Suh et al., 2008; Weiss et al., 2007) The range of that motion can be up to 5 cm (Britton et al., 2007; Seppenwoolde et al., 2002; Shimizu et al., 2001; Suh et al., 2008; Hanley et al., 1999; Keall et al., 2006) in all three principal directions over a time period of a few seconds. The magnitude of the motion and its period are variable from patient to patient, from fraction to fraction and even within each fraction for the same patient. (George et al., 2005; Seppenwoolde et al., 2002; Suh et al., 2008) As a result, the management of tumor (and organ) motion has posed a major challenge for the radiation therapy community in recent years and is still in the phase of research and development.

According to AAPM recommendations (Keall et al., 2006), if a lesion moves in excess of 0.5 cm and if a method for respiratory motion management is available, this method should be applied for treatment planning and delivery. Notably, the report and the references therein stipulate that range of motion, without any explicit explanation where the value of 0.5 cm comes from. A viable possibility is that motion management is recommended when the range of motion becomes comparable to the margin added for a set-up uncertainty. Therefore, if the set-up margin is estimated to be 0.5 cm then the motion management threshold will also be 0.5 cm. With the recent developments in image guidance and patient immobilization though, the set-up margin can probably be reduced to

less than ~0.2 cm to ~0.3 cm, and therefore the connection between set-up margin and gating threshold becomes unsubstantiated. Furthermore, published patient studies, (Seppenwoolde et al., 2002; Shimizu et al., 2001; Starkschall et al., 2004; Suh et al., 2008) discussing the potential benefits of motion management for highly mobile tumors, exclusively concentrate on tumor size and range of tumor motion irrespective of the lesion size and/or location relation to the surrounding critical structures (such as healthy lungs). The detachment between tumor and lung sizes, coupled with the range of tumor motion, is substantiated by the fact that when real patient data is examined meaningful conclusions could be drawn only when a large patient sample is examined. However, all of the published studies (Seppenwoolde et al., 2002; Shimizu et al., 2001; Starkschall et al., 2004; Suh et al., 2008) utilize at most few tens of patients which is quite insufficient to correlate tumor size, range of motion, and lung volume.

*Corresponding author: Ivaylo B. Mihaylov, PhD, Department of Radiation Oncology, Rhode Island Hospital/Brown Medical Center, 593 Eddy St., Providence, RI 02903, Tel: (401) 444-8546; Fax: (401) 444-2149; E-mail: imihaylov@lifespan.org

Received May 04, 2010; Accepted June 08, 2010; Published June 08, 2010

Citation: Mihaylov IB, Lerma FA, Moros EG (2010) Relation Between Tumor Size and Range of Motion in IMRT Treatment Planning for Thoracic Lesions. J Cancer Sci Ther 2: 095-099. doi:10.4172/1948-5956.1000031

Copyright: © 2010 Mihaylov IB, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

This work attempts to shed some light on the relation between the lesion size, its range of motion and their relation to lung volumes. The investigation is based on dosimetric considerations derived from realistic patient treatment plans. It is performed by systematic simulations of target sizes and their ranges of motion. Such investigation has never been published to date and basic relation between size and range of motion for thoracic lesions has not been given in the literature. Understanding the relation among these variables will be very helpful in the evaluation of the available treatment options. Indeed, the motion management approach is highly individualized, but the choice of tumor motion management can not be based only on lesion size and its range of motion. It should also include the relation between the tumor size and range of motion and the lung volumes, as well as the patient tolerability (Keall et al., 2006) for a certain motion management technique.

Materials and Methods

The general idea behind the project is to relate empirically the size of a lesion to its range of motion on the basis of realistic treatment plans where commonly used tissue tolerances are utilized in the treatment planning. The goal was achieved by generating artificial targets with (and without) superimposed motion on real patient computed tomography (CT) scans. IMRT optimization was performed for each scenario. IMRT plans result in more conformal dose distributions than 3D treatment plans. Therefore, the findings in terms of target size and motion range, would be upper limits for the case of 3D conformal radiation therapy. The objectives were to achieve the prescribed doses, subject to the tolerances of the surrounding organs at risk (OARs). For a given prescription dose level the size and/or the range of motion of a lesion was varied until the OAR tolerance doses were reached, given that the prescription was met and the plan was clinically acceptable.

Patient data

Four lung cancer patients, who underwent time-resolved (4D) CT simulations, were retrospectively studied. The 4D CT scans were performed on a Philips Big Bore Brilliance multi-slice CT scanner (Philips Medical Systems, Cleveland, OH) interfaced with a Varian (Varian Medical Systems, Palo Alto, CA) real-time position management (v. 1.62) respiratory gating system (Kubo et al., 2000). The patients were scanned under normal respiration. The nominal (combined for both lungs) lung volumes estimated from mid-ventilation (Wolthaus et al., 2008) breathing phase, derived from the 4D CT scans, were 2969 cm³, 4153 cm³, 5029 cm³, and 6000 cm³ respectively. Those volumes were chosen as representative since the average lung volumes for males and females are 5500 cm³ and 4500 cm³ respectively. The patient CT data were used as basis for target definition, treatment plan generation, and dose calculations.

Contouring

A sphere was chosen for the shape of the artificial target, denoted as spherical planning target volume (PTV). In addition, motion in superior-inferior (SI) direction was considered. The SI motion transformed the simulated spherical PTV into a simulated motion-inclusive internal target volume (ITV) as can be seen from the top panel of Figure 1. Spheres with different radii were auto-contoured on the CT images and used as simulated spherical PTVs. The auto-contouring (Mihaylov et al., 2008) was realized through Pinnacle³ scripting language. Spheres were used as shapes of choice since the sphere is the geometric shape with the largest surface area-to-volume ratio, i.e. the smallest surface area that can contain a given

volume. Therefore, any realistic lesion with certain volume will have surface area greater than the considered spherical shapes. Hence, the obtained results would be the lower limits relating tumor size, range of motion, and nominal lung volumes.

In addition to the artificial target volumes, heart, spinal cord and both lungs were contoured as OARs. In the lung contouring process Pinnacle³ (version 8.1x) (Philips Medical Systems, Fitchburg, WI) treatment planning system (TPS) automatic contouring tool was employed. The default CT threshold values were used. The lung contours were visually verified on each slice.

Treatment planning

For each plan an IMRT deliverable (Dogan et al., 2006; Mihaylov and Siebers, 2008; Siebers and Mohan, 2003; Siebers et al., 2002) optimization was performed by Pinnacle's direct machine parameter optimization algorithm. The doses were computed with Pinnacle's Collapsed Cone convolution (Ahnesjo et al., 1987; Mackie et al., 1985) dose calculation algorithm, which has been shown to be adequate in heterogeneous media (Jones and Das, 2005; Paelinck et al., 2005; Vanderstraeten et al., 2006). The treatment plans consisted of nine coplanar, equally spaced, 6MV photon beams. The beam angles were from 0° (posterior, Varian notation) to 200° in 25° increments (cf. bottom panel of Figure 1). The IMRT parameters used for the optimization restricted the maximum number of multi-leaf collimator segments to 180, with each segment being at least 2 cm² in size, with no less than 2 monitor units delivered through that segment.

Three prescription dose levels to 95% of the simulated ITVs (including spherical simulated PTVs) were considered: 60 Gy, 70 Gy, and 80 Gy in 2 Gy per fraction regimen. The chosen fractionation scheme is consistent with most widely used OAR tolerances specified below. For each plan dose coverage to 95% of the simulated ITV with standard deviation of the dose over the PTV of less than 3% (Aaltonen et al., 1997) was deemed as clinically acceptable. These prescription dose levels were applied to the four patients with nominal lung volumes of 2969 cm³, 4153 cm³, 5029 cm³, and 6000 cm³. The size and/or range of motion of each simulated spherical PTV for each patient

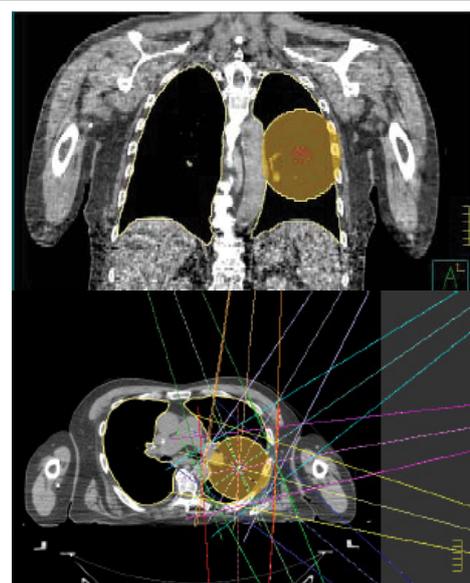


Figure 1: Top: example of simulated spherical (5 cm radius) PTV with superimposed superior-inferior motion of 1.5 cm. Bottom: Beam set-up for 9-field IMRT plans. The nominal lung volume for the presented case is 5029 cm³.

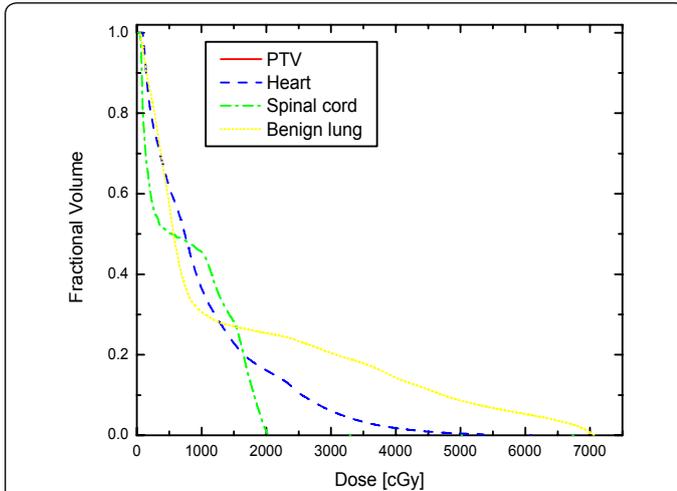


Figure 2: Dose-volume histograms for the case outlined in Figure 1. The prescription dose is 70 Gy to 95% of the simulated ITV for nominal lung volume of 5029 cm³

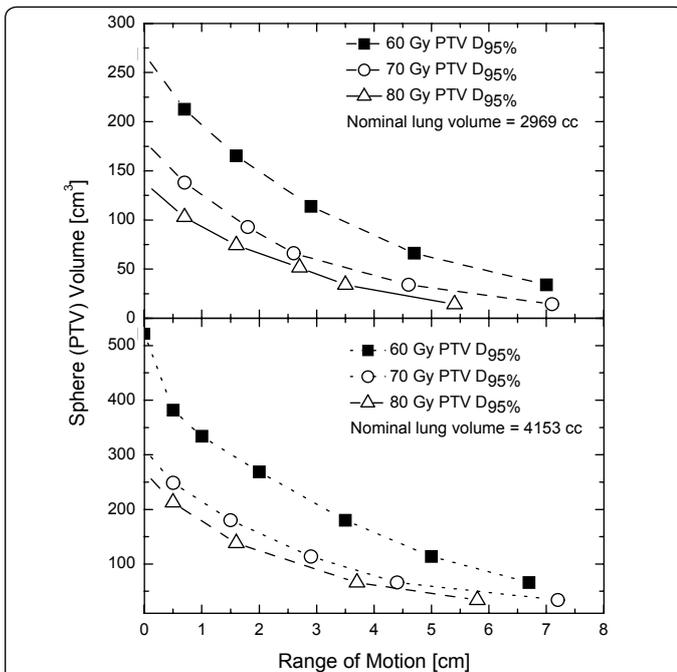


Figure 3: Top: relation between range of motion and a spherical volume corresponding to the simulated PTVs for three dose levels – 60 Gy, 70 Gy, and 80 Gy. The nominal lung volume is 2969 cm³. **Bottom:** relation between range of motion and a spherical volume corresponding to simulated PTV with different radii. Nominal lung volume for this case is 4153 cm³.

and each dose level were varied until abovementioned prescriptions were achieved with the following constraints to the OARs. The dose to 30% of the heart volume (dose index heart $D_{30\%}$) was kept below 40 Gy, together with maximum dose to the heart restricted to the prescription dose (simulated ITV $D_{95\%}$). The dose to 1% of the spinal cord volume (cord $D_{1\%}$) was limited to 40 Gy. The doses to 20% and 30% ($D_{20\%}$ and $D_{30\%}$) of both healthy lungs (excluding the simulated ITV) were limited by 30 Gy and 20 Gy respectively. The simulated ITV were placed (as much as possible) within the left lower lung lobe, thus simulating the worst case scenario where largest amount of benign tissue would be exposed. Thus, the plans will result in the smallest range of motion which will require motion management.

Results

Sample DVHs for the case outlined in Figure 1 are presented in Figure 2. The simulated spherical PTV radius is 5.0 cm with a superimposed range of SI motion of 1.5 cm. The prescription dose is 70 Gy to 95% of the simulated ITV for a nominal lung volume of 5029 cm³. As can be observed from the figure the heart and the spinal cord doses are well below the OAR tolerances used in the IMRT optimization. However, in this particular case 20.41% of the healthy lung tissue is receiving 30 Gy, therefore restricting the simulated spherical PTV size and the imposed range of motion to a sphere with radius of 5.0 cm and a range of motion of 1.5 cm.

A complete set of the simulation results is presented in Figure 3, Figure 4, and Figure 5. Figure 3 and Figure 4 the relations between spherical volumes and range of motion for the four nominal lung volumes are outlined. Details on the lung volumes and dose levels are given in the figure legends. Figure 5 represents the same data as Figure 3 and Figure 4 but in slightly different format. The panels from top to bottom correspond to prescription levels of 60 Gy, 70 Gy, and 80 Gy respectively. Each panel contains four curves where the spherical PTV volumes have been normalized to the nominal lung volumes. It is evident that with an increasing prescription dose the relative tumor volumes, which can be treated without exposing benign lung above tolerances, decrease.

Discussion

This choice of data presentation is dictated by the fact that from a single breathing phase derived from a 4D CT scan (e.g. mid-ventilation (Wolthaus et al., 2008) the size of the tumor and subsequently the size of the PTV can be deduced. From the full inhale and full exhale phases from the other hand the range of motion can be estimated,

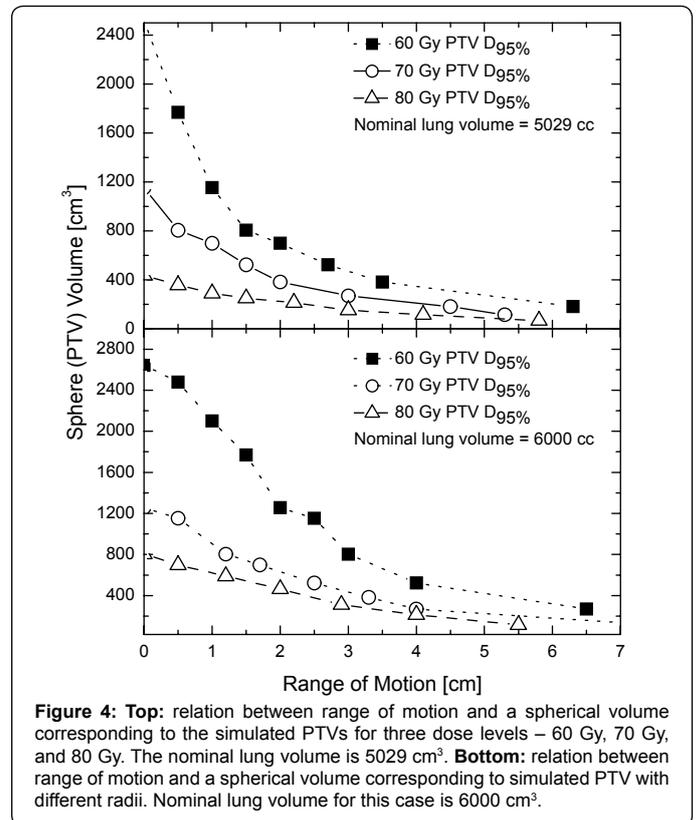


Figure 4: Top: relation between range of motion and a spherical volume corresponding to the simulated PTVs for three dose levels – 60 Gy, 70 Gy, and 80 Gy. The nominal lung volume is 5029 cm³. **Bottom:** relation between range of motion and a spherical volume corresponding to simulated PTV with different radii. Nominal lung volume for this case is 6000 cm³.

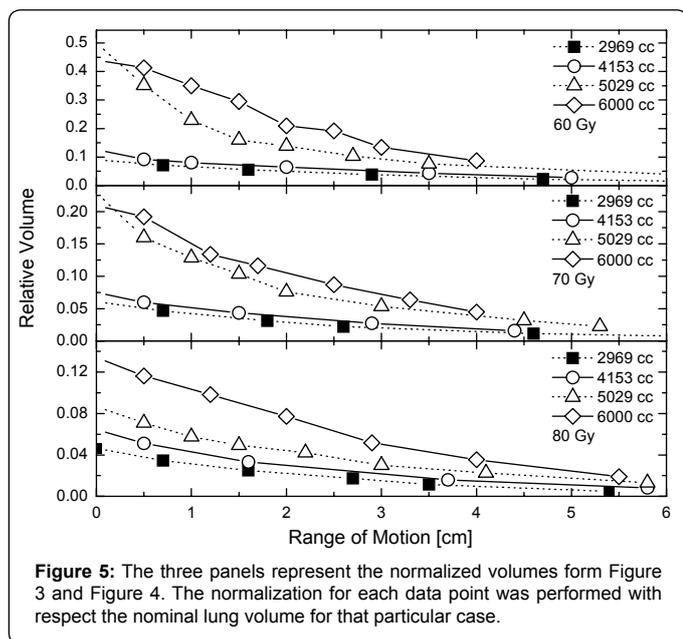


Figure 5: The three panels represent the normalized volumes from Figure 3 and Figure 4. The normalization for each data point was performed with respect to the nominal lung volume for that particular case.

Nominal Volume [cc]	60 [Gy]		70 [Gy]		80 [Gy]	
	A	B	A	B	A	B
3000	-1.05	-0.13	-1.23	-0.15	-1.32	-0.18
4000	-0.94	-0.12	-1.16	-0.13	-1.21	-0.15
5000	-0.44	-0.17	-0.70	-0.18	-1.08	-0.14
6000	-0.32	-0.16	-0.69	-0.14	-0.84	-0.16

Table 1: Power law coefficients A and B used in establishing analytic fits to the curves presented in Figure 5. The relative volumes, corresponding to different radii, can be derived from the power law coefficients by the equation $Relative\ Volume = 10^{(A+B \times range\ of\ motion)}$.

and therefore motion inclusive ITV can be constructed. As a result, the figure can be used as a quick look-up reference for the potential achievable dose level given that lung $D_{20\%}$ and $D_{30\%}$ are not violated. Notably, the presented look-up curves are based solely on lung $D_{20\%}$ and $D_{30\%}$ dose levels.

In addition to the look-up curves analytic fits to the data presented on Figure 5 were performed. The results are presented in Table 1. The graphical data was fitted to a power law of the form $10^{(A+B \times range\ of\ motion)}$, where the “range of motion” is in cm while the result is PTV volume, normalized to the nominal lung volume. The coefficients can be used to calculate the achievable dose levels from a quick estimation of the tumor volume and range of motion obtained from mid-ventilation, end-of-inhale and end-of-exhale phases.

The findings of the work presented herein demonstrate that the motion management threshold of 0.5 cm found in the literature (Keall et al., 2006) is reasonable. The resolution of thoracic CT scans is of the order of 0.3 cm. Therefore, gating threshold of 0.5 cm will almost certainly warrant that motion management is used when it is needed. However, in some cases, depending on the tumor size, tumor range of motion, and total lung volume, it might be too restrictive for a standard (2 Gy per fraction) fractionation scheme. The data presented herein indicates that individualized treatment planning approach should be used to effectively define motion management threshold.

Conclusions

An investigation quantifying the relation between PTV size and its range of motion was presented. IMRT treatment plans were considered, since this technique offers more conformal dose distributions than

conventional 3D treatment technique. The presented results outline upper limits for both IMRT and 3D conformal irradiation, i.e. if PTV volume and/or range of motion is greater (for nominal lung volume) than the simulated sizes, then motion management strategy is necessary in order to limit healthy lung toxicity. The readers must be cautioned of the possibility that the tumor size, and its range of motion for a given nominal lung volume, inferred from the figures or the analytic fits to the data may not be realistic if the lesion is in very close proximity to the heart or the spinal cord where those OARs might be the dose limiting structures.

Acknowledgments

This work was supported in part by Central Arkansas Radiation Therapy Institute (CARTI).

References

- Aaltonen P, Brahme A, Lax I, Leverages S, Naslund I, et al. (1997) Specification of dose delivery in radiation therapy. Recommendation by the Nordic Association of Clinical Physics (NACP). Acta Oncol 36: 1-32.
- Ahnesjo A, Andreo P, Brahme A (1987) Calculation and application of point spread functions for treatment planning with high energy photon beams. Acta Oncol 26: 49-56.
- Britton KR, Starkschall G, Tucker SL, Pan T, Nelson C, et al. (2007) Assessment of gross tumor volume regression and motion changes during radiotherapy for non-small-cell lung cancer as measured by four-dimensional computed tomography. Int J Radiat Oncol Biol Phys 68: 1036-1046.
- Dogan N, Siebers JV, Keall PJ, Lerma F, Wu Y, et al. (2006) Improving IMRT dose accuracy via deliverable Monte Carlo optimization for the treatment of head and neck cancer patients. Med Phys 33: 4033-4043.
- George R, Vedam SS, Chung TD, Ramakrishnan V, Keall PJ (2005) The application of the sinusoidal model to lung cancer patient respiratory motion. Med Phys 32: 2850-2861.
- Hanley J, Debois MM, Mah D, Mageras GS, Raben A, et al. (1999) Deep inspiration breath-hold technique for lung tumors: the potential value of target immobilization and reduced lung density in dose escalation. Int J Radiat Oncol Biol Phys 45: 603-611.
- Ionascu D, Jiang SB, Nishioka S, Shirato H, Berbeco RI (2007) Internal-external correlation investigations of respiratory induced motion of lung tumors. Med Phys 34: 3893-3903.
- Jones AO, Das IJ (2005) Comparison of inhomogeneity correction algorithms in small photon fields. Med Phys 32: 766-776.
- Keall PJ, Mageras GS, Balter JM, Emery RS, Forster KM, et al. (2006) The management of respiratory motion in radiation oncology report of AAPM Task Group 76. Med Phys 33: 3874-3900.
- Kubo HD, Len PM, Minohara S, Mostafavi H (2000) Breathing-synchronized radiotherapy program at the University of California Davis Cancer Center. Med Phys 27: 346-353.
- Mackie TR, Scrimger JW, Battista JJ (1985) A convolution method of calculating dose for 15-MV x rays. Med Phys 12: 188-196.
- Mihaylov IB, Corry P, Yan Y, Ratanatharathorn V, Moros EG (2008) Modeling of carbon fiber couch attenuation properties with a commercial treatment planning system. Med Phys 35: 4982-4988.
- Mihaylov IB, Siebers JV (2008) Evaluation of dose prediction errors and optimization convergence errors of deliverable-based head-and-neck IMRT plans computed with a superposition/convolution dose algorithm. Med Phys 35: 3722-3727.
- Paelinck L, Reynaert N, Thierens H, De Neve W, De Wagter C (2005) Experimental verification of lung dose with radiochromic film: comparison with Monte Carlo simulations and commercially available treatment planning systems. Phys Med Biol 50: 2055-2069.
- Seppenwoolde Y, Shirato H, Kitamura K, Shimizu S, van Herk M, et al. (2002) Precise and real-time measurement of 3D tumor motion in lung due to breathing and heartbeat, measured during radiotherapy. Int J Radiat Oncol Biol Phys 53: 822-834.
- Shimizu S, Shirato H, Ogura S, Akita-Dosaka H, Kitamura K, et al. (2001)

- Detection of lung tumor movement in real-time tumor-tracking radiotherapy. *Int J Radiat Oncol Biol Phys* 51: 304-310.
17. Siebers J, Mohan R (2003) Monte Carlo and IMRT. In: Intensity-Modulated Radiation Therapy. The State of the Art, ed J R Palta and T R Mackie (Colorado Springs, Colorado: Medical Physics Publishing) pp531-561.
18. Siebers JV, Lauterbach M, Keall PJ, Mohan R (2002) Incorporating multi-leaf collimator leaf sequencing into iterative IMRT optimization. *Med Phys* 29: 952-959.
19. Starkschall G, Forster KM, Kitamura K, Cardenas A, Tucker SL, et al. (2004) Correlation of gross tumor volume excursion with potential benefits of respiratory gating. *Int J Radiat Oncol Biol Phys* 60: 1291-1297.
20. Suh Y, Dieterich S, Cho B, Keall PJ (2008) An analysis of thoracic and abdominal tumour motion for stereotactic body radiotherapy patients. *Phys Med Biol* 53: 3623-3640.
21. Vanderstraeten B, Reynaert N, Paelinck L, Madani I, De Wagter C, et al. (2006) Accuracy of patient dose calculation for lung IMRT: A comparison of Monte Carlo, convolution/superposition, and pencil beam computations. *Med Phys* 33: 3149-3158.
22. Weiss E, Wijesooriya K, Dill SV, Keall PJ (2007) Tumor and normal tissue motion in the thorax during respiration: Analysis of volumetric and positional variations using 4D CT. *Int J Radiat Oncol Biol Phys* 67: 296-307.
23. Wolthaus JW, Sonke JJ, van Herk M, Belderbos JS, Rossi MM, et al. (2008) Comparison of different strategies to use four-dimensional computed tomography in treatment planning for lung cancer patients. *Int J Radiat Oncol Biol Phys* 70: 1229-1238.